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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 03/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/821,832	TUSCHL ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-102* is/are pending in the application.

4a) Of the above claim(s) *6-11,13-15,17-42,44-47,51-71,96 and 102* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,12,16,43,48-50 and 72-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action and amendment filed on October 8, 2003 has been entered.

2. Claims are 76-102 are added. Claims 1-5, 12, 16, 42-43, 48-50, 72-95 are considered for examination. Claims 6-11, 13-15, 17-41, 44-47, 51-71, 96, 102 are withdrawn.

3. This application is filed on March 30, 2001 and claims benefit of US provisional applications 60/265,232 filed on 1/31/2001 and 60/193,594 filed on 3/30/2000.

Response to Arguments

4. Applicant's response to the office action (Paper No.8) is fully considered and is found persuasive in part.

5. With reference to the rejection made in the previous office action under 35 USC 112, first paragraph, Applicants' arguments are fully considered and found not persuasive.

Applicants' argue that the structural information or common attributes are disclose in the instant claims and the biological function is disclosed and hence the rejection is improper. Applicants' arguments are fully considered however, the arguments are not persuasive because the structural limitations are not disclosed. The instant claims are broadly drawn to any fragment of a length from about 21 to about 23 nucleotides that mediates RNA interference, which also includes any variant fragment by permutations and combination (by deletion, substitution, addition or alteration of one or more nucleotides). However, the structural limitation (specific sequence identity), that is, the specific binding site sequence or the specified sequence location of RNA of a length from about 21 to about 23 nucleotides, where the biological function is situated that promotes the RNA interference, is not described. Applicants' also argue that the

location of the biological function in the 21 to 23 nt RNA sequence is sufficiently disclosed in the specification and directs Examiners' attention to specific page numbers of the instant specification.

Applicants' arguments are fully considered and found not persuasive because it is noted that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The instant claims do not recite structural limitation (sequence identity or SEQ ID Nos.) and specification is not be read into the claims. Therefore the instant claims do not meet written description guidelines and hence the rejection is maintained herein.

6. With regard to the rejection made in the previous office action under 35 USC 102(b), Applicants arguments have been fully considered and rejection is moot in view of the amendment and new grounds of rejection.

7. With regard to the rejection made in the previous office action under 35 USC 103(a), Applicants arguments have been fully considered and rejection is moot in view of the amendment and new grounds of rejection.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 76-95 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 76-95 are drawn to isolated double stranded RNA and DNA encoding double-stranded RNA of from 21 to about 23 nucleotides that mediates RNA interference of an mRNA to which it corresponds. The instant claims further comprise any fragment of a length from about 21 to about 23 nucleotides that mediates RNA interference, which includes millions of thousands of variant fragment by permutations and combination (by the language- deletion, substitution, addition or alteration of one or more nucleotides). The written description guidelines note regarding such genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here no structural limitation (specific sequence identity), that is, the specific binding site sequence or the specified sequence location of RNA of a length from about 21 to about 23 nucleotides, where the biological function is situated that promotes the RNA interference, is described.

With regard to the written description, all of the claims drawn to an analog of isolated RNA, or an isolated DNA encoding said RNA, encompass different structural limitations, for which, no structural limitation is provided in the specification. It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining

it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In this application at the time of filing, there is no record or description, which would demonstrate conception or written description of any structural information of isolated RNA or an analog of an isolated RNA or isolated DNA encoding said RNA with retaining correlative function in the claimed product.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

A. Claims 76-95 are rejected under 35 U.S.C. 102(e) as being anticipated by Fire et al. (US 6,506,559).

Fire et al. teach an isolated double-stranded RNA of claim 76, 86, of at least 25 nucleotides, (which comprise RNA from about 21 to about 23 nucleotides) that mediate RNA interference of an mRNA to which it corresponds (column 4, lines 23-28, 41-53, column 7, lines 42-52, column 8, lines 1-6, column 14, lines 44-67, column 15, lines 1-30);

With regard to claim 77, 87, Fire et al teach that the RNA comprises 3' terminal hydroxyl group (ribonucleotides) (see column 4, lines 41-46);

With regard to claim, 80, 90, Fire et al. teach that the said RNA inactivates a corresponding gene by transcriptional silencing (see column 6, lines 44-67, column 7, lines 1-52);

With regard to claims 78-79, 88-89, Fire et al. also teach that the RNA comprises chemically synthesized or analog which differs from RNA by addition, deletion, substitution or alteration (see column 7, lines 53-67);

With regard to claim 81, Fire et al. teach a pharmaceutical composition comprising said double-stranded RNA and an appropriate carrier (see column 14, lines 17-31);

With regard to claim 86, 91, Fire et al. teach that isolated RNA is obtained from double-stranded RNA that has been cleaved into sense and antisense fragments of about 21 to about 23 nucleotides (see column 15, lines 10-30, lines 57-61).

With regard to claims 82- 84, 92-94, Fire et al. also disclose isolated DNA comprising DNA encoding said double-stranded RNA (see column 20, lines 19-25, table. 1);

With regard to claims 85, 95, Fire et al. also teach that the DNA encoding said RNA is processed from eukaryotic cells and result in RNA segments of a protein degradation (see column 20, lines 26-40).

Thus the disclosure of Fire et al. meets the limitations in the instant claims.

B. Claims 1, 3-5, 12, 16, 42, 48-50, 76, 78-86, 88-95 are rejected under 35 U.S.C. 102(e) as being anticipated by Baulcombe et al. (USPN. 6,531,647).

Baulcombe et al. teach an isolated RNA of claim 1, 12, 16, 76, of about 14 to 23 nucleotides , (which comprise RNA from about 21 to about 23 nucleotides) that mediates RNA

interference of an mRNA to which it corresponds (see column 7, lines 38-44, column 6, lines 40-45, column 12, lines 47-53);

With regard to claim 5, 80, 90, Baulcombe et al. teach that the said RNA inactivates a corresponding gene by transcriptional silencing (see column 5, lines 33-52, column 6, lines 10-21);

With regard to claims, 1, 76, Baulcombe et al. et al. also teach that the RNA is a double-stranded RNA or single-stranded (see column 6, lines 40-45);

With regard to claims 3-4, 78-79, 88-89, Baulcombe et al. also teach that the RNA comprises chemically synthesized or analog which differs from RNA by addition, deletion, substitution or alteration (see column 6, lines 45-54, column 12, lines 47-53);

With regard to claim 86, 91, Baulcombe et al. teach that isolated RNA is obtained from double-stranded RNA that has been cleaved into sense and antisense fragments of about 21 to about 23 nucleotides (see column 6, lines 40-45, column 7, lines 6-20).

With regard to claims 42, 82- 84, 92-94, Baulcombe et al. also disclose isolated DNA comprising DNA encoding said double-stranded RNA (see column 11, lines 60-63, column 12, lines 47-53);

With regard to claims 85, 95, Baulcombe et al. also teach that the DNA encoding said RNA is processed from eukaryotic cells and result in RNA segments of a protein degradation (see column 7, lines 6-20).

Thus the disclosure of Baulcombe et al. meets the limitations in the instant claims.

C. Claims 1-5, 12, 16, 43, 76-95 are rejected under 35 U.S.C. 102(e) as being anticipated by Morrissey et al. (US 2003/0206887).

Morrissey et al. teach an isolated RNA of claim 1, 12, 16, 76, of about 19 to 25 nucleotides , which comprise RNA from about 21 to about 23 nucleotides) that mediates RNA interference of an mRNA to which it corresponds (see page 6, paragraph 0049, page 7, paragraph 0054, page 10, paragraphs 0074, 0075);

With regard to claim 2, 77, 87, Morrissey et al teach that the RNA comprises 3' terminal hydroxyl group (see page 6, paragraph 0051, page 19, paragraph 0159);

With regard to claim 5, 80, 90, Morrissey et al. teach that the said RNA inactivates a corresponding gene by transcriptional silencing (see page 6, lines 1-4 of paragraph 0049);

With regard to claim 76, Morrissey et al. also teach that the RNA is a double-stranded RNA (see page 6, paragraph 0049);

With regard to claims 3-4, 78-79, 88-89, Morrissey et al. also teach that the RNA comprises chemically synthesized or analog which differs from RNA by addition, deletion, substitution or alteration (3' terminal mononucleotide, dinucleotide, or trinulceotide overhangs) (see page 6, lines 7-12 of paragraph 0049, paragraph 0050);

With regard to claim 81, Morrissey et al. teach a pharmaceutical composition comprising said double-stranded RNA and an appropriate carrier (see page 28, paragraph 0249);

With regard to claim 86, 91, Morrissey et al. teach that isolated RNA is obtained from double-stranded RNA that has been cleaved into sense and antisense fragments of about 21 to about 23 nucleotides (see page 6, lines 12-15 of paragraph 0047).

With regard to claims 82- 84, 92-94, Morrissey et al. also disclose isolated DNA comprising DNA encoding said double-stranded RNA (see page 57, column 1, claims 2-6);

With regard to claims 85, 95, Morrissey et al. also teach that the DNA encoding said RNA is processed from eukaryotic cells and result in RNA segments of a protein degradation (see page 5, paragraph 0046).

Thus the disclosure of Morrissey et al. meets the limitations in the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baulcombe et al. (USPN. 6,531,647) in view of Tally et al. (USPN. 6,475,726).

Baulcombe et al. teach an isolated RNA of claim 1, 12, 16, 76, of about 14 to 23 nucleotides, (which comprise RNA from about 21 to about 23 nucleotides) that mediates RNA

interference of an mRNA to which it corresponds (see column 7, lines 38-44, column 6, lines 40-45, column 12, lines 47-53); Baulcombe et al. teach that the said RNA inactivates a corresponding gene by transcriptional silencing (see column 5, lines 33-52, column 6, lines 10-21); the RNA is a double-stranded RNA or single-stranded (see column 6, lines 40-45); With regard to claim 86, 91, Baulcombe et al. teach that isolation of said RNA (see column 6, lines 40-45, column 7, lines 6-20) and isolated DNA comprising DNA encoding said double-stranded RNA (see column 11, lines 60-63, column 12, lines 47-53).

However Baulcombe et al. did not teach the process of isolation and purification of said RNA.

Tally et al. teach a method for identifying a compound that modulates (inhibit or enhance) the function of a component of a cell (see column 3, lines 14-24), wherein the compound or the biomolecule is isolated and purified using non-denaturing gel electrophoresis and non-denaturing column chromatography (see column 8, lines 35-49).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine isolated RNA as taught by Baulcombe et al. with process of isolation and purification as taught by Tally et al. to achieve expected advantage of developing a purified biomolecule because Tally et al. taught that isolation and purification using the non-denaturing methods would yield a biomolecule of purity to essential homogeneity (see column 8, lines 43-49). An ordinary practitioner would have been motivated to combine the product of Baulcombe et al. with the purification processes as taught by Tally et al. to improve the purity of the isolated biomolecule.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
March 10, 2004

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
3/11/04